SEQUENCE LISTING

| <110> Faustus Forschungs Cie. Translational Cancer Research GmbH | |
|---|---|
| <120> Antisense oligonucleotides for treating proliferating cells | |
| <130> PA32470US-01938 | |
| <140> US/09/700,906 <141> 2001-02-26 NOV 0:8 2002 | |
| <150> DE 198 22 954.2 <151> 1998-05-22 TECH CENTER 1600/2900 | 0 |
| <160> 5 | |
| <170> PatentIn Vers. 2.0 | |
| <210> 1 <211> 12493 <212> DNA <213> Homo sapiens | |
| <220> <221> CDS <222> (197)(9964) | |
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| aatttgcttc tggccttccc ctacggatta tacctggcct tcccctacgg attatactca 180 | |
| acttactgtt tagaaa atg tgg ccc acg aga cgc ctg gtt act atc aaa agg 232 Met Trp Pro Thr Arg Arg Leu Val Thr Ile Lys Arg 1 5 10 | |
| agc ggg gtc gac ggt ccc cac ttt ccc ctg agc ctc agc acc tgc ttg 280 Ser Gly Val Asp Gly Pro His Phe Pro Leu Ser Leu Ser Thr Cys Leu 15 20 25 | |
| ttt gga agg ggt att gaa tgt gac atc cgt atc cag ctt cct gtt gtg 328 Phe Gly Arg Gly Ile Glu Cys Asp Ile Arg Ile Gln Leu Pro Val Val 30 35 40 | |
| tca aaa caa cat tgc aaa gtt gaa atc cat gag cag gag gca ata tta 376 Ser Lys Gln His Cys Lys Val Glu Ile His Glu Gln Glu Ala Ile Leu 45 50 55 60 | |

| | | | | | | | | | | | | | | gtt Val 75 | | 424 |
|-----|-----|-----|-----|-----|---|-----|-----|-----|-----|-----|---|-----|---|-------------------|---|------|
| _ | | | _ | | | | | | _ | _ | | | | att Ile | _ | 472 |
| - | | | | | | | | | | | | | | aag Lys | | 520 |
| | | | | | | | | | | | | | | cgt Arg | | 568 |
| | _ | | - | | | | _ | | | | | | | gat Asp | | 616 |
| _ | _ | | | | | | _ | | | _ | | | | cct Pro 155 | | 664 |
| _ | | | _ | | _ | | - | - | _ | | _ | - | | tca Ser | | 712 |
| _ | _ | _ | _ | | | | | | _ | | | | | cat His | | 760 |
| Gly | Arg | Asn | Gly | Arg | | Āla | Ala | Asp | Pro | Ile | | Gly | | ttt Phe | | 808 |
| _ | | | _ | _ | | | | _ | _ | | | _ | _ | aag Lys | | 856 |
| - | | | | | _ | | _ | | _ | | | | | tct Ser 235 | | 904 |
| | | _ | | | | | | _ | | | _ | _ | _ | aaa Lys | | 952 |
| | | | | | | | | | | | | | | caa Gln | | 1000 |

| _ | | _ | | | | | _ | _ | _ | | | | G1y 999 | | 1048 |
|---|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-------------------|-----|------|
| | | | | | | | | | | | | | Gly 999 | | 1096 |
| | | | | | | | | | | | | | gac Asp | | 1144 |
| | | | | | | | | | | | | | agc Ser 330 | | 1192 |
| | | _ | _ | | | | | | _ | _ | | | aag Lys | | 1240 |
| | | | | | | | | | | | | | aag Lys | | 1288 |
| | | | | | | | | | | | | | ggt Gly | | 1336 |
| _ | | | | | | | | | | | | | aag Lys | | 1384 |
| | Arg | Asn | Arg | Thr | Pro | Ala | Lys | Val | Glu | Asp | Ala | Ala | gac Asp 410 | Ser | 1432 |
| | | | | | | | | | | | | | att Ile | | 1480 |
| | | | | | | | | | | | | | gag Glu | | 1528 |
| | | _ | | | | | _ | | | | | | aag Lys | | 1576 |
| | | | | | | | | | | | | | atg Met | | 1624 |

ggg tta cct ggt ctt agt tca gtt gat atc aac aac ttt ggt gat tcc Gly Leu Pro Gly Leu Ser Ser Val Asp Ile Asn Asn Phe Gly Asp Ser att aat gag agt gag gga ata cct ttg aaa aga agg cgt gtg tcc ttt Ile Asn Glu Ser Glu Gly Ile Pro Leu Lys Arg Arg Arg Val Ser Phe ggt ggg cac cta aga cct gaa cta ttt gat gaa aac ttg cct cct aat Gly Gly His Leu Arg Pro Glu Leu Phe Asp Glu Asn Leu Pro Pro Asn acg cct ctc aaa agg gga gaa gcc cca acc aaa aga aag tct ctg gta Thr Pro Leu Lys Arg Gly Glu Ala Pro Thr Lys Arg Lys Ser Leu Val atq cac act cca cct qtc ctq aaq aaa atc atc aag gaa cag cct caa Met His Thr Pro Pro Val Leu Lys Lys Ile Ile Lys Glu Gln Pro Gln cca tca gga aaa caa gag tca ggt tca gaa atc cat gtg gaa gtg aag Pro Ser Gly Lys Gln Glu Ser Gly Ser Glu Ile His Val Glu Val Lys qca caa aqc ttq gtt ata agc cct cca gct cct agt cct agg aaa act Ala Gln Ser Leu Val Ile Ser Pro Pro Ala Pro Ser Pro Arg Lys Thr cca gtt gcc agt gat caa cgc cgt agg tcc tgc aaa aca gcc cct gct Pro Val Ala Ser Asp Gln Arg Arg Ser Cys Lys Thr Ala Pro Ala tcc agc agc aaa tct cag aca gag gtt cct aag aga gga gga gaa aga Ser Ser Ser Lys Ser Gln Thr Glu Val Pro Lys Arg Gly Glu Arg gtg gca acc tgc ctt caa aag aga gtg tct atc agc cga agt caa cat Val Ala Thr Cys Leu Gln Lys Arg Val Ser Ile Ser Arg Ser Gln His gat att tta cag atg ata tgt tcc aaa aga aga agt ggt gct tcg gaa Asp Ile Leu Gln Met Ile Cys Ser Lys Arg Arg Ser Gly Ala Ser Glu gca aat ctg att gtt gca aaa tca tgg gca gat gta gta aaa ctt ggt Ala Asn Leu Ile Val Ala Lys Ser Trp Ala Asp Val Val Lys Leu Gly

gca aaa caa aca caa act aaa gtc ata aaa cat ggt cct caa agg tca

| Ala | Lys 670 | Gln | Thr | Gln | Thr | Lys 675 | Val | Ile | Lys | His | Gly 680 | Pro | Gln | Arg | Ser | |
|-----|------------|-----|-----|-----|-----|------------|-----|-----|-----|-----|-------------------|-----|-----|-----|-----|------|
| | | | | | | | | | | | aag Lys | | | | | 2296 |
| _ | _ | | - | | | - | | | | | aac Asn | | | | | 2344 |
| | | | | | | | | | | | cat His | | | | | 2392 |
| | | | | | | | | | | | caa Gln | | | | | 2440 |
| | | | | | | | | | | | aag Lys 760 | | | | | 2488 |
| | | | | | | | | | | | gct Ala | | | | | 2536 |
| | | | | | | | | | | | gat Asp | | | | | 2584 |
| | | | | | | | | | | | aat Asn | | | | | 2632 |
| _ | _ | | - | _ | | | | | | | tgc Cys | | | | | 2680 |
| | | | | | | | | | | | aac Asn 840 | | | | | 2728 |
| | ~ ~ | | | | | _ | | | _ | | aca Thr | | | | | 2776 |
| | | | - | | | | | | | | gta Val | | | | | 2824 |

| | | | | | | | | _ | _ | | | | | agt Ser | | 2872 |
|------------|------------|-------------------|------------|------------|------------|------------|-------------------|------------|------------|------------|------------|-------------------|------------|--------------------|------------|------|
| | | | | | | | | | | | | | | aga Arg | | 2920 |
| | | | | | | | | | | | | | | aag Lys | | 2968 |
| | | | | | | | | | | | | | | aaa Lys | | 3016 |
| | _ | _ | _ | _ | | _ | _ | _ | _ | | _ | | | 999 Gly 955 | _ | 3064 |
| | | | | | | | | | | | | | | cct Pro | | 3112 |
| aca Thr | gaa Glu | ctc Leu 975 | atg Met | aaa Lys | gac Asp | acg Thr | gca Ala 980 | cgt Arg | ggc Gly | cag Gln | aat Asn | ctc Leu 985 | ctc Leu | caa Gln | acc Thr | 3160 |
| | _ | | _ | _ | _ | | _ | _ | _ | Lys | | | | act Thr | | 3208 |
| _ | Pro | _ | _ | Ser | Leu | Gln | Pro | _ | Pro | | Asn | | | aca Thr | | 3256 |
| | | | Gln | | | | | Leu | | | | | Val | aaa Lys 1035 | | 3304 |
| | | Leu | | | | | Phe | | | | | Gly | | acc Thr | | 3352 |
| | Thr | | | | | Ala | | | | | Ser | | | acg Thr | | 3400 |
| Lys | | | | | Gln | | | | | Āla | | | | act Thr | | 3448 |

| atg aag aag tgg co Met Lys Lys Trp Pr 1085 | | | | 96 |
|--|-----------------|-------------------|-----------------|-----|
| gac ctg gct ggc tt Asp Leu Ala Gly Ph 110 | e Lys Glu Leu E | | | 44 |
| gaa tca atg act ga Glu Ser Met Thr As 1120 | p Glu Lys Thr T | | | 92 |
| cca cca gaa tca gt Pro Pro Glu Ser Va 1135 | | Thr Ser Thr Lys (| | 40 |
| aga agt ctc agg aa Arg Ser Leu Arg Ly 1150 | | | | 88 |
| aaa cta aca cca to Lys Leu Thr Pro Se 1165 | | | | '36 |
| gga ggt gat gag aa Gly Gly Asp Glu Ly 118 | s Asp Ile Lys A | | | 84 |
| aaa ctg gac ctg go Lys Leu Asp Leu Al 1200 | a Gly Thr Leu H | | | 32 |
| act cct aag gaa aa Thr Pro Lys Glu Ly 1215 | | Leu Glu Asp Leu A | , 33 | 80 |
| gag ctc ttc cag ac Glu Leu Phe Gln Th 1230 | | | , , , , , , , , | 28 |
| aaa acc act aaa at Lys Thr Thr Lys Il 1245 | | | , J-J J | 76 |
| acc cca aca agc ac Thr Pro Thr Ser Th | r Lys Gln Arg I | | | 24 |
| gat gta gag gga ga Asp Val Glu Gly Gl | | | 2 | 72 |

1280 1285 1290

| ggc aaa gcc atg cac acg cct aaa cca tca gta ggt gaa gag aaa gac Gly Lys Ala Met His Thr Pro Lys Pro Ser Val Gly Glu Glu Lys Asp 1295 1300 1305 | 4120 |
|---|------|
| atc atc ata ttt gtg gga act cca gtg cag aaa ctg gac ctg aca gag Ile Ile Ile Phe Val Gly Thr Pro Val Gln Lys Leu Asp Leu Thr Glu 1310 1315 1320 | 4168 |
| aac tta acc ggc agc aag aga cgg cca caa act cct aag gaa gag gccAsn Leu Thr Gly Ser Lys Arg Arg Pro Gln Thr Pro Lys Glu Glu Ala132513301340 | 4216 |
| cag gct ctg gaa gac ctg act ggc ttt aaa gag ctc ttc cag acc cct Gln Ala Leu Glu Asp Leu Thr Gly Phe Lys Glu Leu Phe Gln Thr Pro 1345 1350 1355 | 4264 |
| ggt cat act gaa gaa gca gtg gct gct ggc aaa act act aaa atg ccc Gly His Thr Glu Glu Ala Val Ala Ala Gly Lys Thr Thr Lys Met Pro 1360 1365 1370 | 4312 |
| tgc gaa tct tct cca cca gaa tca gca gac acc cca aca agc aca aga Cys Glu Ser Ser Pro Pro Glu Ser Ala Asp Thr Pro Thr Ser Thr Arg 1375 1380 1385 | 4360 |
| agg cag ccc aag aca cct ttg gag aaa agg gac gta cag aag gag ctc Arg Gln Pro Lys Thr Pro Leu Glu Lys Arg Asp Val Gln Lys Glu Leu 1390 1395 1400 | 4408 |
| tca gcc ctg aag aag ctc aca cag aca tca ggg gaa acc aca cac Ser Ala Leu Lys Lys Leu Thr Gln Thr Ser Gly Glu Thr Thr His Thr 1405 1410 1415 1420 | 4456 |
| gat aaa gta cca gga ggt gag gat aaa agc atc aac gcg ttt agg gaa Asp Lys Val Pro Gly Gly Glu Asp Lys Ser Ile Asn Ala Phe Arg Glu 1425 1430 1435 | 4504 |
| act gca aaa cag aaa ctg gac cca gca gca agt gta act ggt agc aag Thr Ala Lys Gln Lys Leu Asp Pro Ala Ala Ser Val Thr Gly Ser Lys 1440 1445 1450 | 4552 |
| agg cac cca aaa act aag gaa aag gcc caa ccc cta gaa gac ctg gct Arg His Pro Lys Thr Lys Glu Lys Ala Gln Pro Leu Glu Asp Leu Ala 1455 1460 1465 | 4600 |
| ggc tgg aaa gag ctc ttc cag aca cca gta tgc act gac aag ccc acg Gly Trp Lys Glu Leu Phe Gln Thr Pro Val Cys Thr Asp Lys Pro Thr 1470 1475 1480 | 4648 |
| act cac gag aaa act acc aaa ata gcc tgc aga tca caa cca gac cca | 4696 |

| Thr His Glu 1485 | Lys Thr Thr Lys 1490 | - | Arg Ser Gln Pro 195 | Asp Pro 1500 |
|---------------------|--|---------------|------------------------|-----------------|
| ~ ~ ~ | cca aca agc tcc Pro Thr Ser Ser 1505 | _ | Ser Lys Arg Ser | |
| Lys Val Asp | gta gaa gaa gaa Val Glu Glu Glu 1520 | | | |
| | aaa gcc atg cac Lys Ala Met His | | | |
| | tac gca ttt atg Tyr Ala Phe Met 1555 | | | |
| | tta act ggc agc Leu Thr Gly Ser 1570 | Lys Arg Arg I | | |
| | gct cta gaa gac Ala Leu Glu Asp 1585 | | Phe Lys Glu Leu | |
| Thr Arg Gly | cac act gag gaa His Thr Glu Glu 1600 | _ | | |
| | aaa tct tca caa Lys Ser Ser Gln | | | |
| | cgg ctc aag aca Arg Leu Lys Thr 1635 | | | |
| | gca gtt ggc aag Ala Val Gly Lys 1650 | Leu Thr Gln 7 | | |
| | aca gag cca aca Thr Glu Pro Thr 1665 | | Lys Ser Met Lys | |
| Met Glu Ser | cca aag cag atc Pro Lys Gln Ile 1680 | | | |

| agc aag agg cag ctg Ser Lys Arg Gln Let 1695 | | | |
|--|------------------|-------------------|-------------|
| gac ctg gcc ggc ttc Asp Leu Ala Gly Phe 1710 | | | |
| gaa tca atg act aat Glu Ser Met Thr Asr 1725 | | | |
| cag cca gac cta gto Gln Pro Asp Leu Val 1745 | . Asp Thr Pro Th | | |
| aga agt ctc agg aaa Arg Ser Leu Arg Lys 1760 | | u Glu Glu Phe Leu | |
| aaa caa acg cca tca Lys Gln Thr Pro Ser 1775 | | | |
| gta ggt gaa gag aaa Val Gly Glu Glu Lys 1790 | | | |
| aaa ctg gac cag cca Lys Leu Asp Gln Pro 1805 | | | |
| act cgt aag gaa aag Thr Arg Lys Glu Lys 1829 | s Ala Gln Ala Le | | Gly Phe Arg |
| gag ctt ttc cag aca Glu Leu Phe Gln Thr 1840 | | p Asn Pro Thr Ala | |
| act acc aaa aaa ata Thr Thr Lys Lys Ile 1855 | | | |
| acc cca aca aac aca Thr Pro Thr Asn Thi 1870 | = | | |
| gac gta gag gaa gaa Asp Val Glu Glu Glu 1885 | | | |

| ggc aaa gcc atg cac acg cct aaa gca gca gta ggt gaa gag aa Gly Lys Ala Met His Thr Pro Lys Ala Ala Val Gly Glu Glu Ly 1905 1910 191 | ys Asp |
|--|--------|
| atc aac aca ttt gtg ggg act cca gtg gag aaa ctg gac ctg ct Ile Asn Thr Phe Val Gly Thr Pro Val Glu Lys Leu Asp Leu Le 1920 1925 1930 | |
| aat tta cct ggc agc aag aga cgg cca caa act cct aaa gaa aa Asn Leu Pro Gly Ser Lys Arg Arg Pro Gln Thr Pro Lys Glu Ly 1935 1940 1945 | |
| aag gct cta gaa gat ctg gct ggc ttc aaa gag ctc ttc cag ac Lys Ala Leu Glu Asp Leu Ala Gly Phe Lys Glu Leu Phe Gln Th 1950 1960 | |
| ggt cac act gag gaa tca atg acc gat gac aaa atc aca gaa gt Gly His Thr Glu Glu Ser Met Thr Asp Asp Lys Ile Thr Glu Va 1965 1970 1975 | |
| tgc aaa tct cca caa cca gac cca gtc aaa acc cca aca agc tc Cys Lys Ser Pro Gln Pro Asp Pro Val Lys Thr Pro Thr Ser Se 1985 1990 199 | er Lys |
| caa cga ctc aag ata tcc ttg ggg aaa gta ggt gtg aaa gaa ga Gln Arg Leu Lys Ile Ser Leu Gly Lys Val Gly Val Lys Glu Gl 2000 2005 2010 | |
| cta cca gtc ggc aag ctc aca cag acg tca ggg aag acc aca ca Leu Pro Val Gly Lys Leu Thr Gln Thr Ser Gly Lys Thr Thr Gl 2015 2020 2025 | |
| cac aga gag aca gca gga gat gga aag agc atc aaa gcg ttt aa His Arg Glu Thr Ala Gly Asp Gly Lys Ser Ile Lys Ala Phe Ly 2030 2035 2040 | |
| tct gca aag cag atg ctg gac cca gca aac tat gga act ggg at Ser Ala Lys Gln Met Leu Asp Pro Ala Asn Tyr Gly Thr Gly Me 2045 2050 2055 | |
| agg tgg cca aga aca cct aag gaa gag gcc caa tca cta gaa ga Arg Trp Pro Arg Thr Pro Lys Glu Glu Ala Gln Ser Leu Glu As 2065 2070 207 | sp Leu |
| gcc ggc ttc aaa gag ctc ttc cag aca cca gac cac act gag ga Ala Gly Phe Lys Glu Leu Phe Gln Thr Pro Asp His Thr Glu Gl 2080 2085 2090 | |
| aca act gat gac aaa act acc aaa ata gcc tgc aaa tct cca co Thr Thr Asp Asp Lys Thr Thr Lys Ile Ala Cys Lys Ser Pro Pr | |

gaa tca atg gac act cca aca agc aca agg agg cgg ccc aaa aca cct Glu Ser Met Asp Thr Pro Thr Ser Thr Arg Arg Pro Lys Thr Pro ttg ggg aaa agg gat ata gtg gaa gag ctc tca gcc ctg aag cag ctc Leu Gly Lys Arg Asp Ile Val Glu Glu Leu Ser Ala Leu Lys Gln Leu aca cag acc aca cac aca gac aaa gta cca gga gat gag gat aaa ggc Thr Gln Thr Thr His Thr Asp Lys Val Pro Gly Asp Glu Asp Lys Gly atc aac gtg ttc agg gaa act gca aaa cag aaa ctg gac cca gca gca Ile Asn Val Phe Arq Glu Thr Ala Lys Gln Lys Leu Asp Pro Ala Ala agt gta act ggt agc aag agg cag cca aga act cct aag gga aaa gcc Ser Val Thr Gly Ser Lys Arg Gln Pro Arg Thr Pro Lys Gly Lys Ala caa ccc cta gaa gac ttg gct ggc ttg aaa gag ctc ttc cag aca cca Gln Pro Leu Glu Asp Leu Ala Gly Leu Lys Glu Leu Phe Gln Thr Pro gta tgc act gac aag ccc acg act cac gag aaa act acc aaa ata gcc Val Cys Thr Asp Lys Pro Thr Thr His Glu Lys Thr Thr Lys Ile Ala tgc aga tct cca caa cca gac cca gtg ggt acc cca aca atc ttc aag Cys Arg Ser Pro Gln Pro Asp Pro Val Gly Thr Pro Thr Ile Phe Lys cca cag tcc aag aga agt ctc agg aaa gca gac gta gag gaa gaa tcc Pro Gln Ser Lys Arg Ser Leu Arg Lys Ala Asp Val Glu Glu Ser tta gca ctc agg aaa cga aca cca tca gta ggg aaa gct atg gac aca Leu Ala Leu Arg Lys Arg Thr Pro Ser Val Gly Lys Ala Met Asp Thr ccc aaa cca gca gga ggt gat gag aaa gac atg aaa gca ttt atg gga Pro Lys Pro Ala Gly Gly Asp Glu Lys Asp Met Lys Ala Phe Met Gly act cca gtg cag aaa ttg gac ctg cca gga aat tta cct ggc agc aaa Thr Pro Val Gln Lys Leu Asp Leu Pro Gly Asn Leu Pro Gly Ser Lys

aga tgg cca caa act cct aag gaa aag gcc cag gct cta gaa gac ctg

| Arg Trp Pro Gln The | | Ala Gln Ala Leu Glu Asp Leu 2310 2315 |
|---------------------|-------------------|--|
| | | cca ggc act gac aag ccc acg 7192 Pro Gly Thr Asp Lys Pro Thr 2330 |
| | | tgc aaa tct cca caa cca gac 7240 Cys Lys Ser Pro Gln Pro Asp 2345 |
| | | caa cgg ccc aag aga aac ctc 7288 Gln Arg Pro Lys Arg Asn Leu 2360 |
| | | tta gca ctc agg aaa cga aca 7336 Leu Ala Leu Arg Lys Arg Thr 2375 2380 |
| | s Ala Met Asp Thr | cca aaa cca gca gta agt gat 7384 Pro Lys Pro Ala Val Ser Asp 2390 2395 |
| | | act cca gtg cag aaa ctg gac 7432 Thr Pro Val Gln Lys Leu Asp 2410 |
| | | aga cag cca cag act cct aag 7480 Arg Gln Pro Gln Thr Pro Lys 2425 |
| | | gtt ggc ttc aaa gaa ctc ttc 7528 Val Gly Phe Lys Glu Leu Phe 2440 |
| | | atg act gat gac aaa atc aca 7576 Met Thr Asp Asp Lys Ile Thr 2455 2460 |
| | s Ser Pro Gln Pro | gag tca ttc aaa acc tca aga 7624 Glu Ser Phe Lys Thr Ser Arg 2470 2475 |
| | | ctg gtg aaa gtg gac atg aaa 7672 Leu Val Lys Val Asp Met Lys 2490 |
| | | aca cgg aca tca ggg gag act 7720 Thr Arg Thr Ser Gly Glu Thr 2505 |

| acg caa aca cac Thr Gln Thr His 2510 | | | | | 7768 |
|--|-------------|-------------|---------------|----------------|------|
| ttt aag gag tct Phe Lys Glu Ser 2525 | | Ile Leu Asp | | - | 7816 |
| ggt agc agg agg Gly Ser Arg Arg | | | | | 7864 |
| gaa gac ctg gtt Glu Asp Leu Val 2560 | Asp Phe Lys | | Ser Ala Pro (| | 7912 |
| gaa gag tca atg Glu Glu Ser Met 2575 | Thr Ile Asp | | | · - | 7960 |
| ccc cca cca gaa Pro Pro Pro Glu 2590 | | | | | 8008 |
| aag aca cgt ccc Lys Thr Arg Pro 2605 | | Val Lys Glu | | | 8056 |
| agg ctc acg caa Arg Leu Thr Glr | | | | | 8104 |
| gca agc ggt gat Ala Ser Gly Asp 2640 | | Lys Val Leu | Lys Gln Arg A | | 8152 |
| aaa cca aac cca Lys Pro Asn Pro 2655 | Val Glu Glu | | | | 8200 |
| cct aag gaa aag Pro Lys Glu Lys 2670 | | | | | 8248 |
| ctc tct gaa aca Leu Ser Glu Thr 2685 | | Thr Gln Glu | _ | - | 8296 |
| gcc act aaa ata Ala Thr Lys Ile | | | | | 8344 |

| aca gca agc aca a Thr Ala Ser Thr L 2720 | | | | |
|--|---------------|---------------|---------------|---------|
| gta aaa gaa gag c Val Lys Glu Glu P 2735 | | l Lys Phe Th | | |
| acc acg gat gca g Thr Thr Asp Ala A 2750 | - | | | |
| gca ttg aag gaa t Ala Leu Lys Glu S 2765 | | | a Pro Ala Ala | |
| act ggc agc agg a Thr Gly Ser Arg A 27 | rg Arg Pro Ar | | g Glu Ser Ala | |
| ata gaa gac cta g Ile Glu Asp Leu A 2800 | | | | |
| gaa tca atg act g Glu Ser Met Thr A 2815 | _ | r Thr Lys Ile | | |
| cca gaa cta gaa g Pro Glu Leu Glu A 2830 | - | | | |
| cgt gcc cag aaa g Arg Ala Gln Lys V 2845 | al Glu Val Ly | rs Glu Glu Le | | Gly Lys |
| ctc aca caa acc t Leu Thr Gln Thr S 28 | | | r Asp Lys Glu | |
| ggt gag ggc aaa g Gly Glu Gly Lys G 2880 | | | | |
| gtg gac gca gaa g Val Asp Ala Glu A 2895 | | y Ser Arg Arg | | |
| aag gaa aag gcc c Lys Glu Lys Ala G | | | - | |

tet caa aca eca gge cae act gag gaa etg gea aat ggt get get gat Ser Gln Thr Pro Gly His Thr Glu Glu Leu Ala Asn Gly Ala Ala Asp age ttt aca age get eea aag eaa aca eet gae agt gga aaa eet eta Ser Phe Thr Ser Ala Pro Lys Gln Thr Pro Asp Ser Gly Lys Pro Leu aaa ata tcc aga aga gtt ctt cgg gcc cct aaa gta gaa ccc gtg gga Lys Ile Ser Arg Arg Val Leu Arg Ala Pro Lys Val Glu Pro Val Gly qac gtg gta agc acc aga gac cct gta aaa tca caa agc aaa agc aac Asp Val Val Ser Thr Arg Asp Pro Val Lys Ser Gln Ser Lys Ser Asn act tcc ctg ccc cca ctg ccc ttc aag agg gga ggt ggc aaa gat gga Thr Ser Leu Pro Pro Leu Pro Phe Lys Arg Gly Gly Lys Asp Gly age gtc acg gga acc aag agg ctg cgc tgc atg cca gca cca gag gaa Ser Val Thr Gly Thr Lys Arg Leu Arg Cys Met Pro Ala Pro Glu Glu att gtg gag gag ctg cca gcc agc aag aag cag agg gtt gct ccc agg Ile Val Glu Glu Leu Pro Ala Ser Lys Lys Gln Arg Val Ala Pro Arg gca aga ggc aaa tca tcc gaa ccc gtg gtc atc atg aag aga agt ttg Ala Arg Gly Lys Ser Ser Glu Pro Val Val Ile Met Lys Arg Ser Leu agg act tet gea aaa aga att gaa eet geg gaa gag etg aac age aac Arg Thr Ser Ala Lys Arg Ile Glu Pro Ala Glu Glu Leu Asn Ser Asn gac atg aaa acc aac aaa gag gaa cac aaa tta caa gac tcg gtc cct Asp Met Lys Thr Asn Lys Glu Glu His Lys Leu Gln Asp Ser Val Pro gaa aat aag gga ata tcc ctg cgc tcc aga cgc caa gat aag act gag Glu Asn Lys Gly Ile Ser Leu Arg Ser Arg Arg Gln Asp Lys Thr Glu gca gaa caq caa ata act gag gtc ttt gta tta gca gaa aga ata gaa Ala Glu Gln Gln Ile Thr Glu Val Phe Val Leu Ala Glu Arg Ile Glu

ata aac aga aat gaa aag aag ccc atg aag acc tcc cca gag atg gac

•

| Ile Asn Arg Asn Glu Lys Lys Pro Met Lys Thr Ser Pro Glu Met Asp 3120 3125 3130 | |
|---|------|
| att cag aat cca gat gat gga gcc cgg aaa ccc ata cct aga gac aaa 96 Ile Gln Asn Pro Asp Asp Gly Ala Arg Lys Pro Ile Pro Arg Asp Lys 3135 3140 3145 | 540 |
| gtc act gag aac aaa agg tgc ttg agg tct gct aga cag aat gag agc 96 Val Thr Glu Asn Lys Arg Cys Leu Arg Ser Ala Arg Gln Asn Glu Ser 3150 3160 | 88 |
| tcc cag cct aag gtg gca gag gag agc gga ggg cag aag agt gcg aag Ser Gln Pro Lys Val Ala Glu Glu Ser Gly Gly Gln Lys Ser Ala Lys 3165 3170 3175 3180 | 736 |
| gtt ctc atg cag aat cag aaa ggg aaa gga gaa gca gga aat tca gac 97 Val Leu Met Gln Asn Gln Lys Gly Lys Gly Glu Ala Gly Asn Ser Asp 3185 3190 3195 | 784 |
| tcc atg tgc ctg aga tca aga aag aca aaa agc cag cct gca gca agc 98 Ser Met Cys Leu Arg Ser Arg Lys Thr Lys Ser Gln Pro Ala Ala Ser 3200 3205 3210 | 332 |
| act ttg gag agc aaa tct gtg cag aga gta acg cgg agt gtc aag agg 98 Thr Leu Glu Ser Lys Ser Val Gln Arg Val Thr Arg Ser Val Lys Arg 3215 3220 3225 | 880 |
| tgt gca gaa aat cca aag aag gct gag gac aat gtg tgt gtc aag aaa 99 Cys Ala Glu Asn Pro Lys Lys Ala Glu Asp Asn Val Cys Val Lys Lys 3230 3235 3240 | 928 |
| ata aca acc aga agt cat agg gac agt gaa gat att tgacagaaaa 99 Ile Thr Thr Arg Ser His Arg Asp Ser Glu Asp Ile 3245 3250 3255 | 974 |
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| agetttgeag aatgaageet tgaggtetgt caccacccac agecacccta cagcageett 10 | 274 |
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Cys Lys Val Glu Ile His Glu Gln Glu Ala Ile Leu His Asn Phe Ser 50 55 60

Ser Thr Asn Pro Thr Gln Val Asn Gly Ser Val Ile Asp Glu Pro Val 65 70 75 80

Arg Leu Lys His Gly Asp Val Ile Thr Ile Ile Asp Arg Ser Phe Arg 85 90 95

Tyr Glu Asn Glu Ser Leu Gln Asn Gly Arg Lys Ser Thr Glu Phe Pro 100 105 110

Arg Lys Ile Arg Glu Gln Glu Pro Ala Arg Arg Val Ser Arg Ser Ser 115 120 125

Phe Ser Ser Asp Pro Asp Glu Lys Ala Gln Asp Ser Lys Ala Tyr Ser 130 135 140

Lys Ile Thr Glu Gly Lys Val Ser Gly Asn Pro Gln Val His Ile Lys Asn Val Lys Glu Asp Ser Thr Ala Asp Asp Ser Lys Asp Ser Val Ala Gln Gly Thr Thr Asn Val His Ser Ser Glu His Ala Gly Arg Asn Gly Arg Asn Ala Ala Asp Pro Ile Ser Gly Asp Phe Lys Glu Ile Ser Ser Val Lys Leu Val Ser Arg Tyr Gly Glu Leu Lys Ser Val Pro Thr Thr Gln Cys Leu Asp Asn Ser Lys Lys Asn Glu Ser Pro Phe Trp Lys Leu Tyr Glu Ser Val Lys Lys Glu Leu Asp Val Lys Ser Gln Lys Glu Asn Val Leu Gln Tyr Cys Arg Lys Ser Gly Leu Gln Thr Asp Tyr Ala Thr Glu Lys Glu Ser Ala Asp Gly Leu Gln Gly Glu Thr Gln Leu Leu Val Ser Arg Lys Ser Arg Pro Lys Ser Gly Gly Ser Gly His Ala Val Ala Glu Pro Ala Ser Pro Glu Gln Glu Leu Asp Gln Asn Lys Gly Lys Gly Arg Asp Val Glu Ser Val Gln Thr Pro Ser Lys Ala Val Gly Ala Ser Phe Pro Leu Tyr Glu Pro Ala Lys Met Lys Thr Pro Val Gln Tyr Ser Gln Gln Gln Asn Ser Pro Gln Lys His Lys Asn Lys Asp Leu Tyr Thr Thr Gly Arg Arg Glu Ser Val Asn Leu Gly Lys Ser Glu Gly Phe Lys Ala Gly Asp Lys Thr Leu Thr Pro Arg Lys Leu Ser Thr Arg Asn Arg Thr Pro Ala Lys Val Glu Asp Ala Ala Asp Ser Ala Thr Lys Pro Glu

Asn Leu Ser Ser Lys Thr Arg Gly Ser Ile Pro Thr Asp Val Glu Val Leu Pro Thr Glu Thr Glu Ile His Asn Glu Pro Phe Leu Thr Leu Trp Leu Thr Gln Val Glu Arg Lys Ile Gln Lys Asp Ser Leu Ser Lys Pro Glu Lys Leu Gly Thr Thr Ala Gly Gln Met Cys Ser Gly Leu Pro Gly Leu Ser Ser Val Asp Ile Asn Asn Phe Gly Asp Ser Ile Asn Glu Ser Glu Gly Ile Pro Leu Lys Arg Arg Arg Val Ser Phe Gly Gly His Leu Arg Pro Glu Leu Phe Asp Glu Asn Leu Pro Pro Asn Thr Pro Leu Lys Arg Gly Glu Ala Pro Thr Lys Arg Lys Ser Leu Val Met His Thr Pro Pro Val Leu Lys Lys Ile Ile Lys Glu Gln Pro Gln Pro Ser Gly Lys Gln Glu Ser Gly Ser Glu Ile His Val Glu Val Lys Ala Gln Ser Leu Val Ile Ser Pro Pro Ala Pro Ser Pro Arg Lys Thr Pro Val Ala Ser Asp Gln Arg Arg Ser Cys Lys Thr Ala Pro Ala Ser Ser Ser Lys Ser Gln Thr Glu Val Pro Lys Arg Gly Glu Arg Val Ala Thr Cys Leu Gln Lys Arg Val Ser Ile Ser Arg Ser Gln His Asp Ile Leu Gln Met Ile Cys Ser Lys Arg Arg Ser Gly Ala Ser Glu Ala Asn Leu Ile Val Ala Lys Ser Trp Ala Asp Val Val Lys Leu Gly Ala Lys Gln Thr Gln Thr Lys Val Ile Lys His Gly Pro Gln Arg Ser Met Asn Lys Arg

Gln Arg Arg Pro Ala Thr Pro Lys Lys Pro Val Gly Glu Val His Ser Gln Phe Ser Thr Gly His Ala Asn Ser Pro Cys Thr Ile Ile Ile Gly Lys Ala His Thr Glu Lys Val His Val Pro Ala Arg Pro Tyr Arg Val Leu Asn Asn Phe Ile Ser Asn Gln Lys Met Asp Phe Lys Glu Asp Leu Ser Gly Ile Ala Glu Met Phe Lys Thr Pro Val Lys Glu Gln Pro Gln Leu Thr Ser Thr Cys His Ile Ala Ile Ser Asn Ser Glu Asn Leu Leu Gly Lys Gln Phe Gln Gly Thr Asp Ser Gly Glu Glu Pro Leu Leu Pro Thr Ser Glu Ser Phe Gly Gly Asn Val Phe Phe Ser Ala Gln Asn Ala Ala Lys Gln Pro Ser Asp Lys Cys Ser Ala Ser Pro Pro Leu Arg Arg Gln Cys Ile Arg Glu Asn Gly Asn Val Ala Lys Thr Pro Arg Asn Thr Tyr Lys Met Thr Ser Leu Glu Thr Lys Thr Ser Asp Thr Glu Thr Glu Pro Ser Lys Thr Val Ser Thr Val Asn Arg Ser Gly Arg Ser Thr Glu Phe Arg Asn Ile Gln Lys Leu Pro Val Glu Ser Lys Ser Glu Glu Thr Asn Thr Glu Ile Val Glu Cys Ile Leu Lys Arg Gly Gln Lys Ala Thr Leu Leu Gln Gln Arg Arg Glu Gly Glu Met Lys Glu Ile Glu Arg Pro Phe Glu Thr Tyr Lys Glu Asn Ile Glu Leu Lys Glu Asn Asp Glu Lys Met Lys Ala Met Lys Arg Ser Arg Thr Trp Gly Gln Lys Cys Ala Pro

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- Lys Asp Thr Ala Arg Gly Gln Asn Leu Leu Gln Thr Gln Asp His Ala 980 985 990
- Lys Ala Pro Lys Ser Glu Lys Gly Lys Ile Thr Lys Met Pro Cys Gln 995 1000 1005
- Ser Leu Gln Pro Glu Pro Ile Asn Thr Pro Thr His Thr Lys Gln Gln 1010 1015 1020
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- Thr Pro Gly His Thr Glu Glu Leu Val Ala Ala Gly Lys Thr Thr Lys 1235 1240 1245
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- Thr Pro Leu Glu Lys Arg Asp Val Gln Lys Glu Leu Ser Ala Leu Lys 1395 1400 1405
- Lys Leu Thr Gln Thr Ser Gly Glu Thr Thr His Thr Asp Lys Val Pro 1410 1415 1420
- Gly Glu Asp Lys Ser Ile Asn Ala Phe Arg Glu Thr Ala Lys Gln 1425 1430 1435 1440
- Lys Leu Asp Pro Ala Ala Ser Val Thr Gly Ser Lys Arg His Pro Lys 1445 1450 1455
- Thr Lys Glu Lys Ala Gln Pro Leu Glu Asp Leu Ala Gly Trp Lys Glu 1460 1465 1470
- Leu Phe Gln Thr Pro Val Cys Thr Asp Lys Pro Thr Thr His Glu Lys 1475 1480 1485
- Thr Thr Lys Ile Ala Cys Arg Ser Gln Pro Asp Pro Val Asp Thr Pro 1490 1495 1500

- Thr Ser Ser Lys Pro Gln Ser Lys Arg Ser Leu Arg Lys Val Asp Val 1505 1510 1515 1520
- Glu Glu Glu Phe Phe Ala Leu Arg Lys Arg Thr Pro Ser Ala Gly Lys 1525 1530 1535
- Ala Met His Thr Pro Lys Pro Ala Val Ser Gly Glu Lys Asn Ile Tyr 1540 1550
- Ala Phe Met Gly Thr Pro Val Gln Lys Leu Asp Leu Thr Glu Asn Leu 1555 1560 1565
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- Leu Glu Asp Leu Ala Gly Phe Lys Glu Leu Phe Gln Thr Arg Gly His 1585 1590 1595 1600
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- Ser Ser Gln Pro Asp Leu Asp Lys Asn Pro Ala Ser Ser Lys Arg Arg 1620 1630
- Leu Lys Thr Ser Leu Gly Lys Val Gly Val Lys Glu Glu Leu Leu Ala 1635 1640 1645
- Val Gly Lys Leu Thr Gln Thr Ser Gly Glu Thr Thr His Thr His Thr 1650 1655 1660
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- Asn Glu Lys Thr Thr Lys Val Ser Tyr Arg Ala Ser Gln Pro Asp Leu 1730 1735 1740
- Val Asp Thr Pro Thr Ser Ser Lys Pro Gln Pro Lys Arg Ser Leu Arg 1745 1750 1755 1760
- Lys Ala Asp Thr Glu Glu Glu Phe Leu Ala Phe Arg Lys Gln Thr Pro 1765 1770 1775

- Ser Ala Gly Lys Ala Met His Thr Pro Lys Pro Ala Val Gly Glu Glu 1780 1785 1790
- Lys Asp Ile Asn Thr Phe Leu Gly Thr Pro Val Gln Lys Leu Asp Gln 1795 1800 1805
- Pro Gly Asn Leu Pro Gly Ser Asn Arg Arg Leu Gln Thr Arg Lys Glu 1810 1815 1820
- Lys Ala Gln Ala Leu Glu Glu Leu Thr Gly Phe Arg Glu Leu Phe Gln 1825 1830 1835 1840
- Thr Pro Cys Thr Asp Asn Pro Thr Ala Asp Glu Lys Thr Thr Lys Lys 1845 1850 1855
- Ile Leu Cys Lys Ser Pro Gln Ser Asp Pro Ala Asp Thr Pro Thr Asn 1860 1865 1870
- Thr Lys Gln Arg Pro Lys Arg Ser Leu Lys Lys Ala Asp Val Glu Glu 1875 1880 1885
- Glu Phe Leu Ala Phe Arg Lys Leu Thr Pro Ser Ala Gly Lys Ala Met 1890 1895 1900
- His Thr Pro Lys Ala Ala Val Gly Glu Glu Lys Asp Ile Asn Thr Phe 1905 1910 1915 1920
- Val Gly Thr Pro Val Glu Lys Leu Asp Leu Leu Gly Asn Leu Pro Gly
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- Ser Lys Arg Arg Pro Gln Thr Pro Lys Glu Lys Ala Lys Ala Leu Glu 1940 1945 1950
- Asp Leu Ala Gly Phe Lys Glu Leu Phe Gln Thr Pro Gly His Thr Glu 1955 1960 1965
- Glu Ser Met Thr Asp Asp Lys Ile Thr Glu Val Ser Cys Lys Ser Pro 1970 1975 1980
- Gln Pro Asp Pro Val Lys Thr Pro Thr Ser Ser Lys Gln Arg Leu Lys 1985 1990 1995 2000
- Ile Ser Leu Gly Lys Val Gly Val Lys Glu Glu Val Leu Pro Val Gly
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- Lys Leu Thr Gln Thr Ser Gly Lys Thr Thr Gln Thr His Arg Glu Thr 2020 2025 2030
- Ala Gly Asp Gly Lys Ser Ile Lys Ala Phe Lys Glu Ser Ala Lys Gln 2035 2040 2045

- Met Leu Asp Pro Ala Asn Tyr Gly Thr Gly Met Glu Arg Trp Pro Arg 2050 2055 2060
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- Ile Thr Glu Val Phe Val Leu Ala Glu Arg Ile Glu Ile Asn Arg Asn 3105 3110 3115 3120
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